

I. AMENDMENTS

AMENDMENTS TO THE CLAIMS

Cancel claims 13, 22, 23, 26-29, 33-38, and 40-61 without prejudice to renewal.

Please enter the amendments to claims 1, 5, 6, 24, and 25, as shown below.

Please enter new claims 64-97, as shown below.

1. **(Currently amended)** A method of identifying a gene product having activity in a terpene biosynthetic pathway, the method comprising:

a) producing a test cell by introducing into a genetically modified host cell an exogenous nucleic acid comprising a nucleotide sequence encoding a candidate gene product, wherein the genetically modified host cell is genetically modified with one or more nucleic acids that comprise nucleotide sequences encoding one or more of acetoacetyl-CoA thiolase, hydroxymethylglutaryl-CoA synthase, hydroxymethylglutaryl-CoA reductase, mevalonate kinase, phosphomevalonate kinase, and mevalonate pyrophosphate decarboxylase, wherein said genetic modification results in production of ~~produces a terpene biosynthetic pathway intermediate, wherein the intermediate is a prenyl diphosphate, and which~~ a prenyl diphosphate intermediate is produced in an amount effective to inhibit growth of the genetically modified host cell; and

b) determining the effect, if any, of expression of the candidate gene product on growth of the test cell, wherein a reduction in growth inhibition indicates the candidate gene product has activity in the terpene biosynthetic pathway.

2. **(Original)** The method of claim 1, wherein the exogenous nucleic acid comprises nucleotide sequences encoding two or more gene products.

3. **(Original)** The method of claim 1, wherein the exogenous nucleic acid is isolated from a cell of a species that is different from the genetically modified host cell.

4. **(Original)** The method of claim 3, wherein the exogenous nucleic acid is isolated from a eukaryotic cell or a prokaryotic cell.

5. **(Currently amended)** The method of claim 3, wherein the exogenous nucleic acid is isolated from a cell of an organism selected from a protozoan, a plant, a fungus, an algae ~~alga~~, a yeast, a reptile, an amphibian, a mammal, a marine microorganism, a marine invertebrate, an arthropod, an isopod, an insect, an arachnid, an archaeobacterium, and a cubacterium.

6. **(Currently amended)** The method of claim 5 [[3]], wherein the genome of the organism is mutated prior to isolation of nucleic acid from the organism.
7. (Original) The method of claim 1, wherein the exogenous nucleic acid is a cDNA.
8. (Original) The method of claim 1, wherein the exogenous nucleic acid is a cDNA library.
9. (Original) The method of claim 1, wherein the exogenous nucleic acid is genomic DNA.
10. (Original) The method of claim 1, wherein the exogenous nucleic acid is a genomic DNA library.
11. (Original) The method of claim 1, wherein the exogenous nucleic acid is synthetic DNA.
12. (Original) The method of claim 11, wherein the synthetic DNA is amplified using a polymerase chain reaction.
13. **(Cancelled)**
14. (Original) The method of claim 1, wherein the genetically modified host cell is a prokaryotic cell.
15. (Original) The method of claim 14, wherein the prokaryotic cell is *Escherichia coli*.
16. (Original) The method of claim 1, wherein the genetically modified host cell is a eukaryotic cell.
17. (Original) The method of claim 16, wherein the eukaryotic cell is a yeast cell.
18. (Original) The method of claim 17, wherein the yeast cell is *Saccharomyces cerevisiae*.
19. (Original) The method of claim 1, further comprising isolating the exogenous nucleic acid from the test cell.

20. (Original) The method of claim 1, further comprising separating growth-inhibited test cells from test cells that exhibit a reduction in growth inhibition by buoyant density separation; and isolating the exogenous nucleic acid from the test cells that exhibit reduced growth inhibition.

21.-23. (Cancelled)

24. (Currently amended) The method of claim 1 [[22]], wherein the genetically modified host cell is further genetically modified with one or more nucleic acids that comprise nucleotide sequences encoding one or more of acetoacetyl-CoA thiolase, hydroxymethylglutaryl-CoA synthase, hydroxymethylglutaryl-CoA reductase, mevalonate kinase, phosphomevalonate kinase, mevalonate pyrophosphate decarboxylase, and a nucleic acid comprising a nucleotide sequence encoding an isopentenyl pyrophosphate isomerase.

25. (Currently amended) The method of claim 1 [[22]], wherein the genetically modified host cell is further genetically modified with one or more nucleic acids that comprise nucleotide sequences encoding acetoacetyl-CoA thiolase, hydroxymethylglutaryl-CoA synthase, hydroxymethylglutaryl-CoA reductase, mevalonate kinase, phosphomevalonate kinase, mevalonate pyrophosphate decarboxylase, isopentenyl pyrophosphate isomerase, and a nucleic acid comprising a nucleotide sequence encoding a prenyl transferase.

26.-29. (Cancelled)

30. (Previously presented) The method of claim 1, wherein the prenyl diphosphate is a monoprenyl diphosphate.

31. (Previously presented) The method of claim 1, wherein the prenyl diphosphate is a polyprenyl diphosphate.

32. (Original) The method of claim 31, wherein the polyprenyl diphosphate is selected from geranyl diphosphate, farnesyl diphosphate, geranylgeranyl diphosphate, geranylfarnesyl diphosphate, hexaprenyl diphosphate, heptaprenyl diphosphate, octaprenyl diphosphate, solanesyl diphosphate, and decaprenyl diphosphate.

33.-38. (Cancelled)

39. (Original) The method of claim 1, wherein the determining step is by monitoring optical density of a liquid culture comprising the test cell, or by identifying a viable test cell.

40.-63. (Cancelled)

64. (New) A method of identifying a gene product having activity in a terpene biosynthetic pathway, the method comprising:

a) producing a test cell by introducing into a genetically modified host cell an exogenous nucleic acid comprising a nucleotide sequence encoding a candidate gene product, wherein the genetically modified host cell is genetically modified with one or more nucleic acids comprising nucleotide sequence encoding mevalonate kinase, phosphomevalonate kinase, and mevalonate pyrophosphate decarboxylase, wherein the genetically modified host cell is cultured in the presence of mevalonate, and wherein said genetic modification results in production of a prenyl diphosphate intermediate in an amount effective to inhibit growth of the genetically modified host cell; and

b) determining the effect, if any, of expression of the candidate gene product on growth of the test cell, wherein a reduction in growth inhibition indicates the candidate gene product has activity in the terpene biosynthetic pathway.

65. (New) The method of claim 64, wherein the genetically modified host cell is further genetically modified with a nucleic acid comprising a nucleotide sequence encoding an isopentenyl pyrophosphate isomerase.

66. (New) The method of claim 64, wherein the genetically modified host cell is further genetically modified with a nucleic acid comprising a nucleotide sequence encoding a prenyl transferase.

67. (New) The method of claim 64, wherein the exogenous nucleic acid is isolated from a cell of a species that is different from the genetically modified host cell.

68. (New) The method of claim 64, wherein the exogenous nucleic acid is isolated from a eukaryotic cell or a prokaryotic cell.

69. (New) The method of claim 64, wherein the exogenous nucleic acid is isolated from a cell of an organism selected from a protozoan, a plant, a fungus, an algae, a yeast, a reptile, an amphibian, a mammal, a marine microorganism, a marine invertebrate, an arthropod, an isopod, an insect, an arachnid, an archaeobacterium, and a eubacterium.

70. (New) The method of claim 69, wherein the genome of the organism is mutated prior to isolation of nucleic acid from the organism.

71. (New) The method of claim 64, wherein the exogenous nucleic acid is a cDNA, a cDNA library, a genomic DNA, a genomic DNA library, or a synthetic DNA.

72. (New) The method of claim 64, wherein the genetically modified host cell is a prokaryotic cell.

73. (New) The method of claim 72, wherein prokaryotic cell is *Escherichia coli*.

74. (New) The method of claim 64, wherein the genetically modified host cell is a eukaryotic cell.

75. (New) The method of claim 74, wherein the eukaryotic cell is a yeast cell.

76. (New) The method of claim 64, further comprising isolating the exogenous nucleic acid from the test cell.

77. (New) The method of claim 64, further comprising separating growth-inhibited test cells from test cells that exhibit a reduction in growth inhibition by buoyant density separation; and isolating the exogenous nucleic acid from the test cells that exhibit reduced growth inhibition.

78. (New) The method of claim 64, wherein the prenyl diphosphate is a monoprenyl diphosphate or a polyprenyl diphosphate.

79. (New) The method of claim 78, wherein the polyprenyl diphosphate is selected from geranyl diphosphate, farnesyl diphosphate, geranylgeranyl diphosphate, geranylarnesyl diphosphate, hexaprenyl diphosphate, heptaprenyl diphosphate, octaprenyl diphosphate, solanesyl diphosphate, and decaprenyl diphosphate.

80. (New) The method of claim 64, wherein the determining step is by monitoring optical density of a liquid culture comprising the test cell, or by identifying a viable test cell.

81. (New) A method of identifying a gene product having activity in a terpene biosynthetic pathway, the method comprising:

a) producing a test cell by introducing into a genetically modified host cell an exogenous nucleic acid comprising a nucleotide sequence encoding a candidate gene product, wherein the genetically modified host cell is genetically modified with one or more nucleic acids comprising nucleotide sequences encoding 4-diphosphocytidyl-2-C-methyl-D-erythritol synthase, 4-diphosphocytidyl-2-C-methyl-D-erythritol kinase, 2C-methyl-D-erythritol 2,4-cyclodiphosphate synthase, 1-hydroxy-2-methyl-2-(*E*)-butenyl 4-diphosphate synthase, and isopentenyl/dimethylallyl diphosphate synthase, and wherein said genetic modification results in production of a prenyl diphosphate intermediate in an amount effective to inhibit growth of the genetically modified host cell; and

b) determining the effect, if any, of expression of the candidate gene product on growth of the test cell, wherein a reduction in growth inhibition indicates the candidate gene product has activity in the terpene biosynthetic pathway.

82. (New) The method of claim 81, wherein the test cell is grown in the presence of methylerythritol.

83. (New) The method of claim 81, wherein the genetically modified host cell is further genetically modified with one or more nucleic acids comprising nucleotide sequences encoding 1-deoxy-D-xylulose-5-phosphate synthase, and 1-deoxy-D-xylulose-5-phosphate reductoisomerase.

84. (New) The method of claim 81, wherein the exogenous nucleic acid is isolated from a cell of a species that is different from the genetically modified host cell.

85. (New) The method of claim 81, wherein the exogenous nucleic acid is isolated from a eukaryotic cell or a prokaryotic cell.

86. (New) The method of claim 81, wherein the exogenous nucleic acid is isolated from a cell of an organism selected from a protozoan, a plant, a fungus, an algae, a yeast, a reptile, an amphibian, a mammal, a marine microorganism, a marine invertebrate, an arthropod, an isopod, an insect, an arachnid, an archaeobacterium, and a eubacterium.

87. (New) The method of claim 86, wherein the genome of the organism is mutated prior to isolation of nucleic acid from the organism.

88. (New) The method of claim 81, wherein the exogenous nucleic acid is a cDNA, a cDNA library, a genomic DNA, a genomic DNA library, or a synthetic DNA.
89. (New) The method of claim 81, wherein the genetically modified host cell is a prokaryotic cell.
90. (New) The method of claim 89, wherein prokaryotic cell is *Escherichia coli*.
91. (New) The method of claim 81, wherein the genetically modified host cell is a eukaryotic cell.
92. (New) The method of claim 91, wherein the eukaryotic cell is a yeast cell.
93. (New) The method of claim 81, further comprising isolating the exogenous nucleic acid from the test cell.
94. (New) The method of claim 81, further comprising separating growth-inhibited test cells from test cells that exhibit a reduction in growth inhibition by buoyant density separation; and isolating the exogenous nucleic acid from the test cells that exhibit reduced growth inhibition.
95. (New) The method of claim 81, wherein the prenyl diphosphate is a monoprenyl diphosphate or a polyprenyl diphosphate.
96. (New) The method of claim 95, wherein the polyprenyl diphosphate is selected from geranyl diphosphate, farnesyl diphosphate, geranylgeranyl diphosphate, geranylarnesyl diphosphate, hexaprenyl diphosphate, heptaprenyl diphosphate, octaprenyl diphosphate, solanesyl diphosphate, and decaprenyl diphosphate.
97. (New) The method of claim 81, wherein the determining step is by monitoring optical density of a liquid culture comprising the test cell, or by identifying a viable test cell.